

09/852,965

-3-

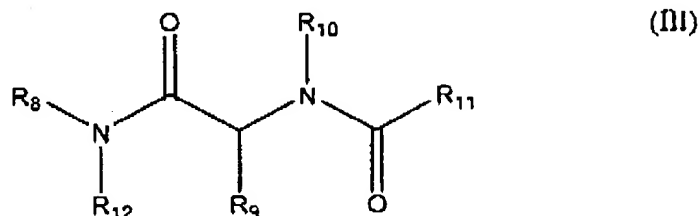
Amendments to the Claims

Please amend Claims 15, 71, 98, 109, 118, 123 and 147. Cancel Claims 86-97, 134-146 and 152-160. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

Claims 1-14 (Cancelled)

15. (Currently Amended) A compound of Formula III,



or a physiologically acceptable salt thereof, wherein:

~~R₈ is a substituted or unsubstituted alkyl; a substituted or unsubstituted aryl; substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;~~

R₈ is an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; a substituted or unsubstituted aryl; an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; an aralkyl or heteroaralkyl substituted in the alkyl portion of the aralkyl or heteroaralkyl with one or more groups selected from fluoro, chloro, bromo, iodo, nitro,

09/852,965

-4-

hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; or an unsubstituted aralkyl or heteroaralkyl;

R₉ is a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R₁₀ is alkyl substituted with NR₁₃R₁₄, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

R₁₁ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenone, or a substituted or unsubstituted cycloalkylalkyl;

R₁₂ is H; and

R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl, and

R₁₅ is -H, an alkyl, an aryl or an aralkyl.

16. (Previously Presented) The compound of Claim 15, wherein R₈ is substituted or unsubstituted phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, linear C₁-C₁₂-alkyl, branched C₁-C₁₂-alkyl, cyclic C₃-C₁₂-alkyl, or dicycloalkyl-C₁-C₄-alkyl.
17. (Previously Presented) The compound of Claim 16, wherein R₈ is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups optionally bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.

09/852,965

-5-

18. (Original) The compound of Claim 17, wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of methoxy, methyl, ethyl and cyano.
19. (Original) The compound of Claim 15, wherein R_x is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.
20. (Original) The compound of Claim 15, wherein R_y is substituted or unsubstituted phenyl, substituted or unsubstituted phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, phenylfuranyl or heteroaryl- C_1 - C_4 -alkyl.
21. (Original) The compound of Claim 20, wherein R_y is phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, C_1 - C_4 -alkyl-S-, a halogen, a halogenated C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, trifluoromethyl, and substituted and unsubstituted phenoxy.
22. (Original) The compound of Claim 20, wherein R_y is phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, methyl, methoxy, phenoxy, chloro-substituted phenoxy, methoxy-substituted phenoxy and methyl-substituted phenoxy.
23. (Original) The compound of Claim 15, wherein R_y is phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, diphenylmethyl, pyrazolylmethyl, 2,4-dimethylphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methyl-4-methoxyphenyl, 3-methyl-4-

09/852,965

-6-

- methoxyphenyl, 4-methylthiophenyl, 3-chlorophenyl, 3-trifluoromethylphenyl, benzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-azidylphenyl, 3-(4-methoxyphenoxy)phenyl, or 5-phenylfuran-2-yl.
24. (Previously Presented) The compound of Claim 15, wherein R_{10} is substituted or unsubstituted phenyl, unsubstituted heteroaraalkyl group, unsubstituted heterocycloalkylalkyl group, or an alkyl substituted with $-NR_{13}R_{14}$.
25. (Original) The compound of Claim 24, wherein R_{10} is 2-(imidazol-4-yl)ethyl, 3-(imidazol-4-yl)propyl, 3-(imidazol-1-yl)propyl, 2-(3-methylimidazol-4-yl)ethyl, 2-(morpholin-4-yl)ethyl, 2-(4-pyrazolyl)ethyl, 4-pyrazolylmethyl, 2-N,N-dimethylaminoethyl, 3-N,N-dimethylaminopropyl, or 2-(aminocarbonyl)phenyl.
26. (Original) The compound of Claim 15, wherein R_{11} is a linear or branched C_1 - C_4 -alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl- C_1 - C_4 -alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl- C_1 - C_4 -alkyl, pyridylcarbonylphenyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl- C_1 - C_4 -alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.
27. (Original) The compound of Claim 26, wherein R_{11} is a phenyl, phenyl- C_1 - C_4 -alkyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, fluorenyl or pyridyl substituted with one or more substituents independently selected from C_1 - C_4 -alkyl and C_1 - C_4 -alkoxy.

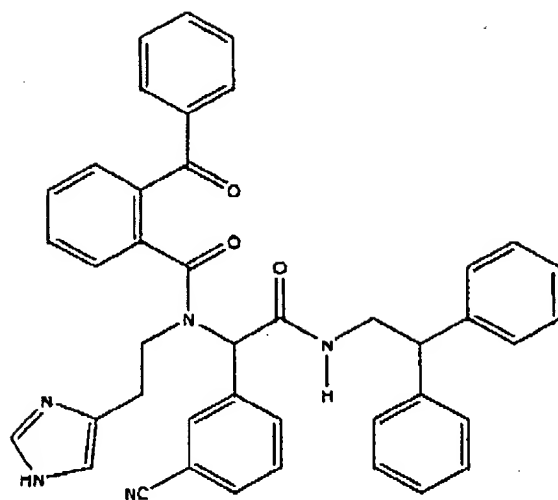
09/852,965

-7-

28. (Original) The compound of Claim 26, wherein R_{11} is a benzophenonyl group, wherein said benzophenonyl group is substituted with a C_1 - C_4 -alkoxy group, a C_1 - C_4 -alkyl group or a chlorine atom.
29. (Original) The compound of Claim 15, wherein R_{11} is benzophenon-2-yl, 4'-methoxybenzophenon-2-yl, 4'-chlorobenzophenon-2-yl, 2-(furan-2-yl)phenyl, 2-(thiophen-2-yl)phenyl, 2-benzylphenyl, 2-pyridylcarbonylphenyl, 2-(phenoxymethyl)phenyl, 2-(*t*-butylcarbonyl)phenyl, 2,2-diphenylethyl, 1-fluorenyl, (naphth-2-yl)methyl, naphth-1-yl, 3-(phenylcarbonyl)propyl, 4-phenylbutyl, 4-butylphenyl, 2-(4-chlorophenylcarbonyl)phenyl, 3-methoxyphenyl, N-methylpyrrol-2-yl, 2,3-dimethoxyphenyl, 3-butyl-2-pyridyl, 2-naphthylmethyl, 2-cyclohexylethyl, 3-methoxyphenyl, N-methyl-2-pyrrolyl, 2-cyclopentylethyl, 3-oxobutyl, 2-benzopyrazyl, quinoxalin-2-yl, 3-idolyl, (2-methylindol-3-yl)methyl, 3-(indol-3-yl)propyl, (indol-3-yl)methyl, (5-bromoindol-3-yl)methyl, 3-chlorophenyl, 3-aminopyrazol-4-yl, 2-(indol-3-yl)-1-hydroxyethyl, 3-fluorophenyl, 1-phenyl-1-hydroxymethyl, 2-phenylphenyl, 2-phenoxypheyl, thiophen-2-yl, or isopropyl.
30. (Previously Presented) A composition comprising an enantiomeric mixture of a compound represented by the following structural formula:

09/852,965

-8-

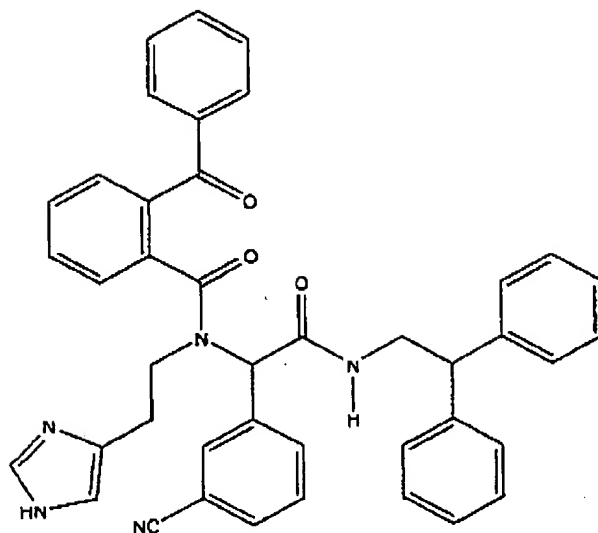


or a physiologically acceptable salt thereof.

31. (Previously Presented) A compound which has a positive specific rotation, wherein the compound is represented by the following structural formula:

09/852,965

-9-

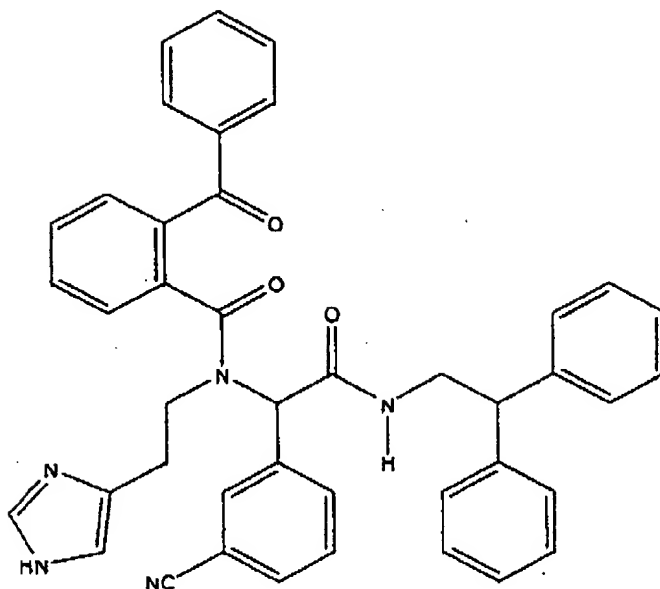


or a physiologically acceptable salt thereof.

32. (Previously Presented) A compound which has a negative specific rotation, wherein the compound is represented by the following structural formula:

09/852,965

-10-



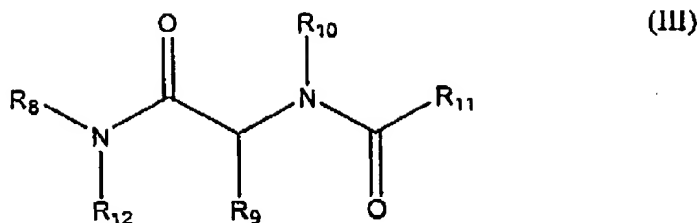
or a physiologically acceptable salt thereof.

Claims 33-70 (Cancelled)

71. (Currently Amended) A method of treating a TNF- α mediated condition in a patient, wherein the TNF-mediated disease is rheumatoid arthritis, sepsis, inflammatory bowel disease, allergic encephalitis or multiple sclerosis, comprising administering to the patient a therapeutically effective amount of a compound of Formula III,

09/852,965

-11-



or a physiologically acceptable salt thereof, wherein:

~~R₈ and R₁₂ are each, independently, H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;~~

R₈ and R₁₂ are each independently H; an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; a substituted or unsubstituted aryl; an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; an aralkyl or heteroaralkyl substituted in the alkyl portion of the aralkyl or heteroaralkyl with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; or an unsubstituted aralkyl or heteroaralkyl;

R₉ is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R₁₀ is alkyl substituted with NR₁₃R₁₄, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

R₁₁ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a

09/852,965

-12-

substituted or unsubstituted benzophenonyl, or a substituted or unsubstituted cycloalkylalkyl; and

R_{13} and R_{14} are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R_{13} and R_{14} together with the nitrogen to which they are attached are a heterocycloalkyl, and

R_{15} is -H, an alkyl, an aryl or an aralkyl.

72. (Original) The method of Claim 71, wherein one of R_8 or R_{12} is -H and the other is substituted or unsubstituted phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, linear C_1 - C_{12} -alkyl, branched C_1 - C_{12} -alkyl, cyclic C_3 - C_{12} -alkyl, or dicycloalkyl- C_1 - C_4 -alkyl.
73. (Original) The method of Claim 72, wherein one of R_8 or R_{12} is -H and the other is phenyl, phenyl- C_1 - C_4 -alkyl, or diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of C_1 - C_4 -alkoxy, C_1 - C_4 -alkyl and cyano.
74. (Original) The method of Claim 73, wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of methoxy, methyl and cyano.
75. (Original) The method of Claim 71, wherein R_8 is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.
76. (Original) The method of Claim 71 wherein R_9 is substituted or unsubstituted phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, phenylfuranyl or heteroaryl- C_1 - C_4 -alkyl.

09/852,965

-13-

77. (Original) The method of Claim 76, wherein R_9 is phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, C_1 - C_4 -alkyl-S-, a halogen C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy, trifluoromethyl, and substituted and unsubstituted phenoxy.
78. (Original) The method of Claim 76, wherein R_9 is phenyl, phenyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of cyano, methyl, methoxy, phenoxy, chloro-substituted phenoxy, methoxy-substituted phenoxy and methyl-substituted phenoxy.
79. (Previously Presented) The method of Claim 71, wherein R_9 is phenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, diphenylmethyl, pyrazolylmethyl, 2,4-dimethylphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methyl-4-methoxyphenyl, 3-methyl-4-methoxyphenyl, 4-methylthiophenyl, 3-chlorophenyl, 3-trifluoromethylphenyl, benzyl, 2-trifluoromethylbenzyl, 3-trifluoromethylbenzyl, 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2-methoxybenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 3-azidylphenyl, 3-(4-methoxyphenoxy)phenyl, or 5-phenylfuran-2-yl.
80. (Previously Presented) The method of Claim 71, wherein R_{10} is substituted or unsubstituted phenyl, unsubstituted heteroaraalkyl group, unsubstituted heterocycloalkylalkyl group, or an alkyl substituted with $-NR_{13}R_{14}$.
81. (Original) The method of Claim 80, wherein R_{10} is 2-(imidazol-4-yl)ethyl, 3-(imidazol-4-yl)propyl, 3-(imidazol-1-yl)propyl 2-(3-methylimidazol-4-yl)ethyl, 2-(morpholin-4-yl)ethyl, 2-(4-pyrazolyl)ethyl, 4-pyrazolylmethyl, 2-N,N-dimethylaminoethyl, 3-N,N-dimethylaminopropyl, and 2-(aminocarbonyl)phenyl.

09/852,965

-14-

82. (Original) The method of Claim 71, wherein R_{11} is a linear or branched C_1 - C_4 -alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl- C_1 - C_4 -alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl- C_1 - C_4 -alkyl, pyridylcarbonylphenyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl- C_1 - C_4 -alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.
83. (Original) The method of Claim 82, wherein R_{11} is a phenyl, phenyl- C_1 - C_4 -alkyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, fluorenyl or pyridyl substituted with one or more substituents independently selected from C_1 - C_4 -alkyl and C_1 - C_4 -alkoxy.
84. (Original) The method of Claim 82, wherein R_{11} is a benzophenonyl group, wherein said benzophenonyl group is substituted with a C_1 - C_4 -alkoxy group, a C_1 - C_4 -alkyl group or a chlorine atom.
85. (Original) The method of Claim 71, wherein R_{11} is benzophenon-2-yl, 4'-methoxybenzophenon-2-yl, 4'-chlorobenzophenon-2-yl, 2-(furan-2-yl)phenyl, 2-(thiophen-2-yl)phenyl, 2-benzylphenyl, 2-pyridylcarbonylphenyl, 2-(phenoxymethyl)phenyl, 2-(*t*-butylcarbonyl)phenyl, 2,2-diphenylethyl, 1-fluorenyl, (naphth-2-yl)methyl, naphth-1-yl, 3-(phenylcarbonyl)propyl, 4-phenylbutyl, 4-butylphenyl, 2-(4-chlorophenylcarbonyl)phenyl, 3-methoxyphenyl, N-methylpyrrol-2-yl, 2,3-dimethoxyphenyl, 3-butyl-2-pyridyl, 2-naphthylmethyl, 2-cyclohexylethyl, 3-methoxyphenyl, N-methyl-2-pyrrolyl, 2-cyclopentylethyl, 3-oxobutyl, 2-benzopyrazyl, quinoxalin-2-yl, 3-idolyl, (2-methylindol-3-yl)methyl, 3-(indol-3-yl)propyl, (indol-3-yl)methyl, (5-bromoindol-3-yl)methyl, 3-chlorophenyl, 3-aminopyrazol-4-yl, 2-(indol-3-

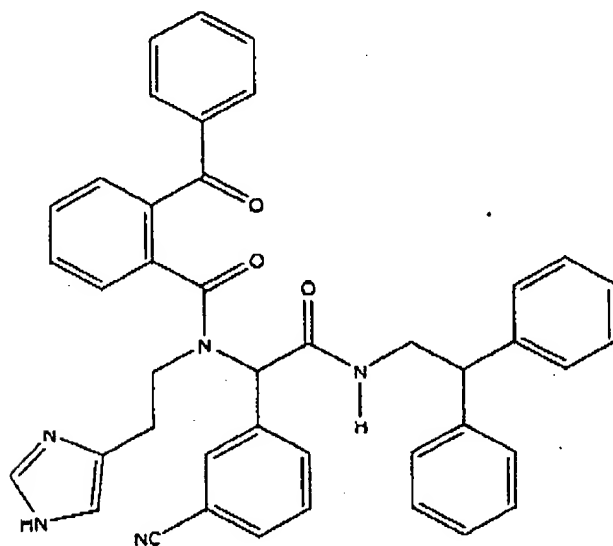
09/852,965

-15-

yl)-1-hydroxyethyl, 3-fluorophenyl, 1-phenyl-1-hydroxymethyl, 2-phenylphenyl, 2-phenoxyphenyl, thiophen-2-yl, or isopropyl.

86-97. (Cancelled)

98. (Currently Amended) A method of treating a TNF- α mediated condition in a patient, wherein the TNF-mediated disease is rheumatoid arthritis, sepsis, inflammatory bowel disease, allergic encephalitis or multiple sclerosis, comprising the step of administering to the patient a therapeutically effective amount of a compound represented by the following structural formula:

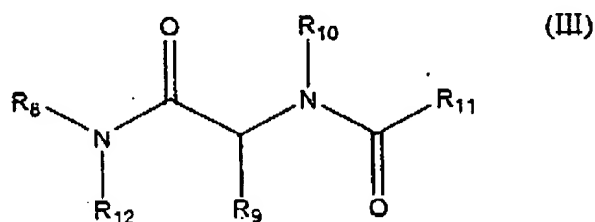


or a physiologically acceptable salt thereof.

09/852,965

-16-

99. (Original) The method of Claim 98, wherein the compound has a positive specific rotation.
100. (Original) The method of Claim 98, wherein the compound has a negative specific rotation.
- 101-108. (Cancelled)
109. (Withdrawn - Currently Amended) A compound according to Formula III:



or a physiologically acceptable salt thereof, wherein;

~~R₈ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl or substituted or unsubstituted heteroaralkyl;~~

R₈ is an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; a substituted or unsubstituted aryl; an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; or an unsubstituted aralkyl or heteroaralkyl;

R₉ is a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R₁₀ is an alkyl substituted with NR₁₃R₁₄ or a substituted or unsubstituted heteroaralkyl;

09/852,965

-17-

R_{11} is a substituted or unsubstituted alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted benzophenone or a substituted or unsubstituted cycloalkyl;

R_{12} is H; and

R_{13} and R_{14} together with the nitrogen to which they are attached are a heterocycloalkyl, and

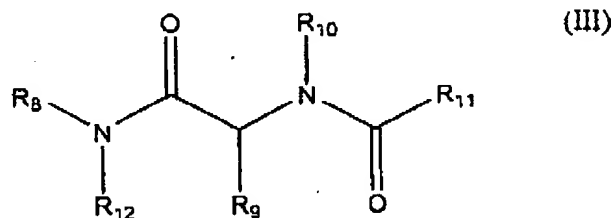
R_{15} is -H, an alkyl, an aryl or an aralkyl.

110. (Withdrawn) A compound according to Claim 109 wherein R_{10} is an unsubstituted heteroaralkyl.
111. (Withdrawn) A compound according to Claim 110 wherein said heteroaralkyl is C_{1-6} alkyl pyridyl, C_{1-6} alkyl pyrimidyl, C_{1-6} alkyl quinolyl, C_{1-6} alkyl isoquinolyl, C_{1-6} alkyl pyrrolyl, C_{1-6} alkyl quinoxalyl, C_{1-6} alkyl imidazolyl, C_{1-6} alkyl oxazolyl, C_{1-6} alkyl isoxazolyl, C_{1-6} alkyl pyrazolyl, C_{1-6} alkyl thienyl, C_{1-6} alkyl furanyl, C_{1-6} alkyl pyrazolyl, C_{1-6} alkyl thiadiazolyl, C_{1-6} alkyl oxadiazolyl, C_{1-6} alkyl indazolyl, C_{1-6} alkyl thiazolyl, C_{1-6} alkyl isothiazolyl, C_{1-6} alkyl tetrazolyl, C_{1-6} alkyl benzo (b) thienyl, C_{1-6} alkyl benzimidazolyl, C_{1-6} alkyl benzoxazolyl, C_{1-6} alkyl benzothiazolyl, C_{1-6} alkyl benzothiadiazolyl, C_{1-6} alkyl benzoxadiazolyl, C_{1-6} alkyl indolyl, C_{1-6} alkyl tetrahydroindolyl, C_{1-6} alkyl azaindolyl, C_{1-6} alkyl indazolyl, C_{1-6} alkyl quinolyl, C_{1-6} alkyl imidazopyridyl, C_{1-6} alkyl puryl, C_{1-6} alkyl pyrrolo[2,3-d]pyrimidyl, C_{1-6} alkyl pyrazolo[3,4-d]pyrimidyl.
112. (Withdrawn) A compound according to Claim 111 wherein R_9 is unsubstituted or substituted aryl.
113. (Withdrawn) A compound according to Claim 112 wherein R_9 is substituted or unsubstituted phenyl.

09/852,965

-18-

114. (Withdrawn) A compound according to Claim 110 wherein R_{11} is an unsubstituted or substituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl- C_1 - C_4 -alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl- C_1 - C_4 -alkyl, pyridylcarbonylphenyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_3 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl- C_1 - C_4 -alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.
115. (Withdrawn) A compound according to Claim 114 wherein R_{11} is unsubstituted or substituted benzophenonyl.
116. (Withdrawn) A compound according to Claim 109 wherein R_8 is phenyl, phenyl- C_1 - C_4 -alkyl, or diphenyl- C_1 - C_4 -alkyl wherein the phenyl group or phenyl groups optionally bear one or more substituents independently selected from the group consisting of C_1 - C_4 -alkoxy, C_1 - C_4 -alkyl and cyano.
117. (Withdrawn) The compound of Claim 116, wherein R_8 is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.
118. (Withdrawn-Currently Amended) A compound according to formula:



09/852,965

-19-

or a physiologically acceptable salt thereof, wherein;

~~R₈ is H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl or substituted or unsubstituted heteroaralkyl;~~

R₈ is an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, -NR₁₃R₁₄, -C(O)R₁₅, cyano and cycloalkyl; a substituted or unsubstituted aryl; an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; or an unsubstituted aralkyl or heteroaralkyl;

R₉ is a substituted or unsubstituted phenyl;

R₁₀ is a C₁-C₆ alkyl imidazolyl;

R₁₁ is a substituted or unsubstituted alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted benzophenone or a substituted or unsubstituted cycloalkyl; and

R₁₂ is H;

R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl, and

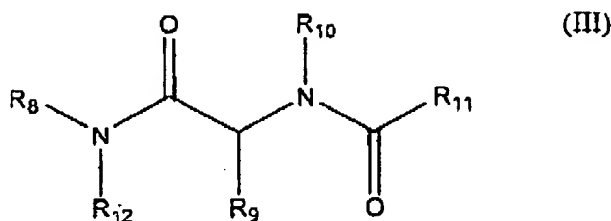
R₁₅ is -H, an alkyl, an aryl or an aralkyl.

119. (Withdrawn) A compound according to Claim 118 wherein R₈ is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.
120. (Withdrawn) The compound of Claim 119, wherein R₈ is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.

09/852,965

-20-

121. (Withdrawn) A compound according to Claim 118 wherein R_{11} is an unsubstituted or substituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl- C_1 - C_4 -alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl- C_1 - C_4 -alkyl, pyridylcarbonylphenyl, phenylcarbonyl- C_1 - C_4 -alkyl, naphthyl, naphthyl- C_1 - C_4 -alkyl, diphenyl- C_1 - C_4 -alkyl, C_5 - C_8 -cycloalkyl- C_1 - C_4 -alkyl, C_1 - C_4 -alkylcarbonyl- C_1 - C_4 -alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.
122. (Withdrawn) A compound according to Claim 121 wherein R_{11} is substituted or unsubstituted benzophenonyl.
123. (Withdrawn-Currently Amended) A method of treating a TNF- α mediated condition in a patient, wherein the TNF-mediated disease is rheumatoid arthritis, sepsis, inflammatory bowel disease, allergic encephalitis or multiple sclerosis, comprising administering to a patient a therapeutically effective amount of:



or a physiologically acceptable salt thereof, wherein

~~R_8 and R_{12} are each independently H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl or substituted or unsubstituted heteroaralkyl;~~

R_8 and R_{12} are each independently H; an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, $-NR_{13}R_{14}$, $-C(O)R_{15}$, cyano and cycloalkyl; a substituted or unsubstituted aryl;

09/852,965

-21-

an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; or an unsubstituted aralkyl or heteroaralkyl;

R_9 is H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

R_{10} is an alkyl substituted with $NR_{13}R_{14}$, or a substituted or unsubstituted heteroaralkyl;

R_{11} is a substituted or unsubstituted alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted benzophenone or a substituted or unsubstituted cycloalkyl; and

R_{13} and R_{14} are each, independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl, or a substituted or unsubstituted aralkyl; or

R_{13} and R_{14} together with the nitrogen to which they are attached are a heterocycloalkyl, and

R_{13} is -H, an alkyl, an aryl or an aralkyl.

- 124 (Withdrawn) The method according to Claim 123 wherein R_{10} is an unsubstituted heteroaralkyl.
125. (Withdrawn) The method according to Claim 124 wherein R_{12} is hydrogen.
126. (Withdrawn) The method according to Claim 125 wherein said heteroaraalkyl is C_{1-6} alkyl pyridyl, C_{1-6} alkyl pyrimidyl, C_{1-6} alkyl quinolyl, C_{1-6} alkyl isoquinolyl, C_{1-6} alkyl pyrrolyl, C_{1-6} alkyl quinoxalyl, C_{1-6} alkyl imidazolyl, C_{1-6} alkyl oxazolyl, C_{1-6} alkyl isoxazolyl, C_{1-6} alkyl pyrazolyl, C_{1-6} alkyl thienyl, C_{1-6} alkyl furanyl, C_{1-6} alkyl pyrazolyl, C_{1-6} alkyl thiadiazolyl, C_{1-6} alkyl oxadiazolyl, C_{1-6} alkyl indazolyl, C_{1-6} alkyl thiazolyl, C_{1-6} alkyl isothiazolyl, C_{1-6} alkyl tetrazolyl, C_{1-6} alkyl benzo (b) thienyl, C_{1-6} alkyl benzimidazolyl,

09/852,965

-22-

C₁₋₆ alkyl benzoxazolyl, C₁₋₆ alkyl benzothiazolyl, C₁₋₆ alkyl benzothiadiazolyl, C₁₋₆ alkyl benzoxadiazolyl, C₁₋₆ alkyl indolyl, C₁₋₆ alkyl tetrahydroindolyl, C₁₋₆ alkyl azaindolyl, C₁₋₆ alkyl indazolyl, C₁₋₆ alkyl quinolinyl, C₁₋₆ alkyl imidazopyridyl, C₁₋₆ alkyl puryl, C₁₋₆ alkyl pyrrolo[2,3-d]pyrimidyl, or C₁₋₆ alkyl pyrazolo[3,4-d]pyrimidyl.

127. (Withdrawn) The method according to Claim 126 wherein R₉ is unsubstituted or substituted aryl.
128. (Withdrawn) The method according to Claim 127 wherein R₉ is substituted or unsubstituted phenyl.
129. (Withdrawn) The method according to Claim 123 wherein R₁₁ is an unsubstituted or substituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl-C₁-C₄-alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl-C₁-C₄-alkyl, pyridylcarbonylphenyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl, naphthyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, C₅-C₈-cycloalkyl-C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl-C₁-C₄-alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.
130. (Withdrawn) The method according to Claim 129 wherein R₁₁ is unsubstituted or substituted benzophenonyl.
131. (Withdrawn) The method according to Claim 123 wherein R₈ is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups optionally bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.

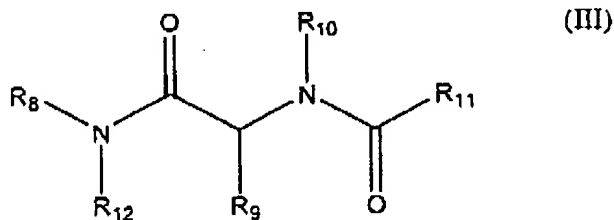
09/852,965

-23-

132. (Withdrawn) The method of Claim 131, wherein the phenyl group or phenyl groups optionally bear one or more substituents independently selected from the group consisting of methoxy, methyl, ethyl and cyano.
133. (Withdrawn) The method of Claim 131, wherein R_8 is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.

134-146. (Cancelled)

147. (Withdrawn-Currently Amended) A method of treating a TNF- α mediated condition in a patient, wherein the TNF-mediated disease is rheumatoid arthritis, sepsis, inflammatory bowel disease, allergic encephalitis or multiple sclerosis, comprising administering to a patient a therapeutically effective amount of formula:



or a physiologically acceptable salt thereof, wherein;

~~R_8 is H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl or substituted or unsubstituted heteroaralkyl;~~

R_8 and R_{12} are each independently H; an unsubstituted alkyl; an alkyl group substituted with one or more groups selected from fluoro, chloro, bromo, iodo, nitro, hydroxyl, $-NR_{13}R_{14}$, $-C(O)R_{15}$, cyano and cycloalkyl; a substituted or unsubstituted aryl;

09/852,965

-24-

an aralkyl substituted in the aromatic portion of the aralkyl; a heteroaralkyl substituted in the heteroaryl portion of the heteroaralkyl; or an unsubstituted aralkyl or heteroaralkyl;

R₉ is a substituted or unsubstituted phenyl;

R₁₀ is a C₁-C₆ alkyl imidazolyl;

R₁₁ is a substituted or unsubstituted alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted benzophenone or a substituted or unsubstituted cycloalkyl; and

R₁₂ is hydrogen; and

R₁₃ and R₁₄ are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl.

148. (Withdrawn) The method according to Claim 147 wherein R₈ is hydrogen and the other is phenyl, phenyl-C₁-C₄-alkyl, or diphenyl-C₁-C₄-alkyl wherein the phenyl group or phenyl groups bear one or more substituents independently selected from the group consisting of C₁-C₄-alkoxy, C₁-C₄-alkyl and cyano.
149. (Withdrawn) The method according Claim 148, wherein R₈ is selected from the group consisting of 2,2-diphenylethyl, 2-(4-ethylphenyl)ethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, 3,4,5-trimethoxybenzyl, 2,4,4-trimethylisopentyl, 2-(4-methoxyphenyl)ethyl, 2-cyclopentyl-2-phenylethyl, or 2-phenyl-2-pyridylethyl.
150. (Withdrawn) The method according to Claim 147 wherein R₁₁ is an unsubstituted or substituted benzophenonyl, pyrazolyl, aminopyrazolyl, substituted or unsubstituted indolyl-C₁-C₄-alkyl, thiophenyl, quinoxaline, substituted or unsubstituted phenyl-C₁-C₄-alkyl, pyridylcarbonylphenyl, phenylcarbonyl-C₁-C₄-alkyl, naphthyl, naphthyl-C₁-C₄-

09/852,965

-25-

alkyl, diphenyl-C₁-C₄-alkyl, C₃-C₈-cycloalkyl-C₁-C₄-alkyl, C₁-C₄-alkylcarbonyl-C₁-C₄-alkyl, fluorenyl, pyrrolyl, N-methylpyrrolyl, or pyridyl.

151. (Withdrawn) The method according to Claim 150 wherein R₁₁ is substituted or unsubstituted benzophenonyl.

152-160 (Cancelled)